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istration of epinephrine, a mixed alpha- and beta-receptor agonist, the resulting coronary perfusion pressure is increased.

Stimulation of vasopressin's V_1 receptor results in vasoconstriction that is mediated through a secondary messenger system different from that used by adrenergic agonists. This holds the promise of synergy when vasopressin is combined with a catecholamine. Vasopressin may decrease oxygen utilization by the myocardium, an effect that is theoretically attractive.

Agent of Choice

Epinephrine has been the pressor of choice in the treatment of refractory cardiac arrest (83,84). There are theoretic reasons to consider the pure alpha agonists, such as phenylephrine, because they raise intravascular pressure without the potentially negative effect on myocardial oxygen utilization. However, animal studies have failed to show a survival advantage when phenylephrine was compared with epinephrine (85). This potential advantage has not resulted in adequate clinical investigation, and at this time, they are rarely used.

Epinephrine, a catecholamine with mixed alpha- and beta-agonist properties, is the agent of choice after failure of defibrillation. Although laboratory and clinical investigations clearly indicate that it can raise perfusion pressure and the rate of ROSC, it has not been unequivocally shown to increase long-term survival. It may be that the paucity of data supporting the use of epinephrine results from the drug being the de facto standard of care for a disease in which performance of placebo-controlled trials is problematic. However, it is possible that the failure of epinephrine, in a range of dosages, to improve long-term survival, may represent a poorly defined toxicity. Clinical trials that indicate toxicity are difficult to interpret because the epinephrine dosage is a strong marker for duration of arrest, which itself is the best predictor of poor outcome.

Recently, there has been considerable interest in the potential utility of vasopressin in the treatment of refractory cardiac arrest. In a series of laboratory and clinical investigations, Lindner et al. (86–90) appear to have demonstrated significantly better outcomes with vasopressin than with epinephrine. There is also the possibility of using vasopressin in combination with adrenergic agonists (91). Further studies are needed.

Route and Dosage

In choosing a route of administration, the clinician must balance timeliness against the potential of greater efficacy. In most cases, epinephrine will be administered as a bolus of 1 mg by peripheral intravenous catheter, followed by a large volume saline flush to assume rapid delivery of the epinephrine into the central circulation.

Although it may be possible to administer the drug more quickly by endotracheal injection, bioavailability may not be adequate. It is possible that increasing the endotracheal dosage may overcome the decreased serum levels obtained by this route. Intracardiac injection is not recommended because intramural administration can reportedly cause intractable VF.

There has been interest in dosages of epinephrine greater than the traditional 1 mg. Laboratory investigations have indicated that higher dosages may improve myocardial blood flow and the rate of ROSC, but that survival may actually be decreased (92). There have been a number of randomized clinical trials of "high dose" epinephrine; in none of these trials was there increased survival, although a meta-analysis has shown improved rate of return of spontaneous circulation (93–95) (Stiell IG. Meta-analysis for high dose epinephrine during CPR. Personal communication, 1999). Epinephrine duration of action is short-lived, so that every 3-min dosing is recommended, although the efficacy of subsequent doses is not well proven.

Potential Alternatives to Standard Closed-Chest Compression

Standard chest compression produces ~25% to 35% of normal cardiac output. There have been exciting developments in CPR adjuncts, for use by health care providers, that appear to improve hemodynamic measurements during resuscitation. These new developments include interposed abdominal compression (IAC) CPR, active compression–decompression CPR, vest CPR, phased chest and abdominal compression–decompression CPR and open-chest CPR.

These techniques have been difficult to study and evaluate definitively for the following reasons: 1) they are often used only late in resuscitation; 2) controversies persist regarding study end points; 3) some of the devices used have not yet received FDA approval; 4) the current health care environment favors conventional therapy and limits experimental procedures; and 5) costs of prospective, randomized trials can be prohibitive.

These alternative forms of resuscitation have solid laboratory data, with some limited clinical data, supporting their efficacy. They also demonstrate an acceptably low incidence of adverse effects. Consideration of the use of these techniques, when approved by the FDA, should come early in the resuscitation effort. Successful use of these techniques requires a commitment to adequate training and follow-up. There is a continual need for randomized trials of such alternatives to prove their efficacy as compared with standard CPR.

Interposed abdominal compression CPR. This type of CPR requires the addition of mid-abdominal compressions by an extra rescuer during the intervals between the chest compressions of conventional CPR (96). The abdominal compression point is located in the midline, halfway between the xiphoid process and the umbilicus. The recommended force of abdominal compression is that sufficient to generate ~100 mm Hg of external pressure on the abdom-

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Table 4. Results of Clinical Studies of Interposed Abdominal Compression Cardiopulmonary Resuscitation (CPR)

Outcome Measure	Studies	IAC CPR	Standard CPR	p Value
Return of spontaneous circulation in or out of the hospital	Mateer (103)	40/145 (28%)	45/146 (31%)	0.54
	Ward (101)	6/16 (38%)	3/17 (18%)	0.19
	Sack (100)	29/48 (60%)	14/55 (25%)	0.00014
	Sack (102)	33/67 (49%)	21/76 (28%)	0.0067
	All four studies	108/276 (39%)	83/294 (28%)	
Return of spontaneous circulation after in-hospital resuscitation	Ward (101)	6/16 (38%)	3/17 (18%)	0.19
	Sack (102)	29/48 (60%)	14/55 (25%)	0.00014
	Sack (104)	33/67 (49%)	21/76 (28%)	0.0067
	All three studies	68/131 (52%)	38/148 (26%)	
Survival to discharge, neurologically intact, after in-hospital resuscitation	Ward (101)	1/16 (6%)	0/17 (0%)	0.3017
	Sack (102)	8/48 (17%)	3/55 (5%)	0.0700
	Both studies	9/64 (14%)	3/72 (4%)	

IAC = interposed abdominal compression.

inal aorta and vena cava and is equivalent to that required to palpate the aortic pulse optimally when the heart is beating normally. Interposed abdominal compression mathematic models generate additional artificial circulation that is approximately equal to that created by chest compressions only (97,98), potentially doubling blood flow during CPR. The positive hemodynamic effects of IAC during CPR have been confirmed in 16 of 17 animal studies using canine and porcine models (99).

Three randomized clinical trials of IAC CPR for in-hospital cardiac arrest have been done (100–102), two of which have shown statistically significant improvement of outcome measures (100,102). One randomized trial of prehospital IAC CPR, combined when possible with standard CPR in the field, showed no difference in outcome (103). These clinical studies are summarized in Table 4. Pooled analysis of all available data for both prehospital and in-hospital resuscitations shows statistically significant improvement in the return of spontaneous circulation with IAC CPR. When only in-hospital studies are examined, the effect of IAC becomes much greater. Pooled data from two studies that examined long-term, neurologically intact survival after in-hospital resuscitations show a positive benefit of IAC CPR as compared with standard CPR. Thus, strong preclinical and clinical evidence supports the use of IAC CPR for in-hospital resuscitations.

Practical implementation of IAC CPR is straightforward and inexpensive. If the chest compressor counts "one—AND—two—AND—three—AND . . . ," the abdominal rescuer applies pressure during "AND." In the hospital, the availability of an extra trained rescuer is rarely a problem.

The safety of IAC, as reviewed previously (104), has been well documented in 426 humans, 151 dogs and 14 pigs. Only one isolated case report of traumatic pancreatitis in a child describes local trauma from abdominal compression during CPR (105). These data compare favorably with the well-known and frequent incidence of rib fracture and pulmonary contusion from chest compression during CPR. Increased emesis and aspiration from IAC have not been reported, and there is evidence that if positive abdominal pressure is applied during ventilations from the beginning of an arrest, the rate of gastric inflation before endotracheal intubation is reduced (106). Review of the available data, therefore, suggests that there is much to be gained and little to be lost from application of IAC CPR during in-hospital resuscitations. Because the most favorable clinical results have been obtained when IAC CPR is applied from the beginning of resuscitation, early application of the technique is to be encouraged. Use of IAC CPR as a last-ditch effort after prolonged, failed ACLS is not recommended.

Active compression–decompression CPR device. Active compression–decompression CPR is a method of CPR utilizing a hand-held suction device to actively compress and then decompress the chest during cardiac arrest. Although chest wall compression achieves the same hemodynamic effect as closed-chest manual CPR, active decompression with the device decreases intrathoracic pressures, leading to enhanced minute ventilation and venous blood return to the thorax. Arterial systolic blood pressure, diastolic blood pressure, coronary perfusion and vital organ perfusion have been shown to be improved in nearly all animal models of VF when ACD CPR is compared with standard CPR (107–110). This increase in overall CPR efficacy led to the development of both a new device (Ambu CardioPump) and the performance of a number of clinical in-hospital and out-of-hospital studies evaluating the potential benefits of this approach.

Results from the clinical trials have been mixed. Although some studies demonstrated no difference between standard CPR and ACD CPR, other clinical trials point to a significant improvement in resuscitation rates and 1 h survival, especially in patients with witnessed cardiac arrests. The most positive results come from Paris, where data demonstrate that one-year survival is doubled with the use of the CardioPump (5%) as compared with standard CPR (<2.0%) (111). In contrast, other large studies have failed to demonstrate any significant outcome improvement with

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ACD (112–115). No study has shown a worse outcome when using ACD CPR as compared with standard CPR. Although ACD CPR has been adopted by the EMS in some countries, preliminary research has shown that the benefits of ACD CPR can be improved by the use of an inspiratory threshold valve (ITV) (116). This valve blocks inspiratory gas exchange during the decompression phase of CPR, thereby augmenting blood return to the chest and overall efficiency of CPR. In patients in prolonged cardiac arrest, use of the combination of ACD CPR plus the ITV resulted in a higher and more rapid rise in end-tidal carbon dioxide and significantly higher systolic and diastolic pressures as compared with ACD CPR alone.

Vest CPR. With vest CPR, a bladder-containing vest (analogous to a large blood pressure cuff) is placed circumferentially around the patient's chest (117). The bladder is inflated and deflated by an automated pneumatic system to cyclically compress the chest. Adherent defibrillation pads can be placed on the chest before applying the vest to allow for defibrillation without the need to remove the vest or interrupt CPR.

Vest CPR was developed as a means of circumferentially compressing the chest with the intention of reducing the thoracic volume and increasing intrathoracic pressure (by Boyle's law) to an extent greater than that which could be achieved with standard manual CPR (118–127). This circumferential compression allows for a large amount of force to be applied without the trauma inherent in applying force to a single point, as with standard chest compression. Laboratory data showed substantial improvement in hemodynamic data and survival.

With the latest improved vest CPR system, hemodynamic measurements in humans were improved significantly over those of standard external chest compression (117). Peak aortic pressure was nearly doubled (up to an average of 138 mm Hg), and coronary perfusion pressure increased by 50%. In addition, 4 of the 29 patients had return of spontaneous circulation during vest CPR, despite their late (50 ± 22 min) resuscitation. In a second phase of the study, patients were randomized to either vest CPR or standard external chest compression after initial resuscitation efforts had failed (11 ± 4 min). There was a trend toward improved initial resuscitation in the vest CPR group, but the trial was too small to show a statistically significant benefit. These data formed the basis for a large-scale, randomized trial of vest CPR immediately after cardiac arrest, which was performed on 81 patients in Europe and showed a trend toward improved survival with vest CPR (128).

Vest CPR requires a sophisticated device for its administration. The technique will obviously be limited to locations where the device would be readily available, although a portable device may be possible. Application of the vest itself is not difficult and can be performed successfully by nurses given only a few minutes of instruction on its use. It is likely that if vest CPR proves successful in improving survival from cardiac arrest, it will remain predominately in the hands of health care professionals. Currently, the vest CPR system is too heavy and consumes too much energy to be easily portable, as would be needed for treating out-of-hospital cardiac arrest victims. The final utility of vest CPR will be determined by the outcomes of larger clinical trials and by whether the device can be miniaturized sufficiently for routine clinical use.

Phased chest and abdominal compression–decompression CPR. This technique incorporates chest compression–decompression and ACD. A manually operated Lifestick Resuscitator (Datascope, Fairfield, New Jersey) is employed. The chest and abdomen are reciprocally compressed and decompressed in a see-saw fashion.

Experimental studies demonstrated impressive hemodynamic efficacy. The coronary perfusion pressure generated by the Lifestick Resuscitator was threefold greater than that generated by conventional precordial compression after 7 min of untreated VF. This was associated with improved initial resuscitability and 72 h survival (129). Experimental studies also indicated that the Lifestick Resuscitator markedly improves efficiency and achieves greater myocardial blood flow, cerebral blood flow (130) and minute ventilation (131), with significantly lower compression force. Hemodynamic efficacy was also demonstrated in a human case series (132).

Open-chest CPR. Open-chest CPR, once the only treatment option for victims of sudden cardiac arrest, quickly fell out of favor with the advent of closed-chest resuscitation techniques. Recognition of the generally poor hemodynamic support generated with closed-chest CPR has spurred a resurgence of interest in invasive forms of CPR.

Previous experimental work in both animals and humans has shown improved CPR-generated hemodynamic data and blood flow with direct cardiac massage. The fundamental unresolved issue is whether the improved hemodynamic data will translate into an improved resuscitation outcome. A number of laboratory experiments have shown an improved outcome with the use of open-chest cardiac massage. An important aspect in employing any invasive CPR method is the time of application within the course of cardiac arrest and the preceding resuscitation efforts. Although open-chest massage may be superior to all forms of closed-chest efforts, because of the inherent morbidity of the associated emergent thoracotomy, it seems most reasonable to try an initial period of closed-chest compressions followed, as soon as possible, by external defibrillation attempts. If successful, the morbidity of the emergent entry into the chest is avoided. Experimental studies of cardiac arrest with open-chest CPR have documented improved coronary perfusion pressures, regardless of when it was begun, but outcome was only improved when invasive CPR was begun within 15 min of the onset of cardiac arrest (133). These findings indicate that invasive techniques such

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as open-chest massage must be applied early, before extensive myocardial injury occurs.

Limited human trials have confirmed the importance of this "window of efficacy" for the successful use of invasive CPR after unsuccessful standard closed-chest compressions. Geehr et al. (134) reported a small series of 49 patients with out-of-hospital cardiac arrest who were randomized to standard closed-chest CPR versus initial closed-chest CPR followed by emergent thoracotomy and open-chest massage on arrival to the hospital. In this study, no survival benefit was seen with the addition of open-chest massage. Scrutiny of the times elapsed before the institution of invasive CPR shows that none of the subjects received open-chest cardiac massage within the first 20 to 25 min of their cardiac arrest. Two recent nonrandomized human studies of open-chest resuscitation confirm the superiority of open-chest direct cardiac massage for hemodynamic support during cardiac arrest and highlight the importance of total cardiac arrest time on successful outcome with invasive CPR (135,136).

Alternative invasive techniques for resuscitation have been developed, many of which have been carefully studied in the past. With either direct mechanical ventricular assistance or emergency cardiopulmonary bypass, the principal issue remains the time to successful application in the arrested patient. Generally, the more sophisticated the device, the more difficult it is to use in a timely fashion during cardiac arrest. One simplified concept that has evolved recently is "minimally invasive direct cardiac massage." Using only a limited 2-cm thoracotomy, a wand-like device is inserted to directly compress the heart. The hope is that by avoiding the necessary thoracotomy of typical open-chest massage, the morbidity will be less and the technique more acceptable. Studies of efficacy are currently under way.

EVALUATION AND CARE AFTER RESUSCITATION

Most patients who are initially resuscitated die within 72 h from persistent postresuscitation cerebral or myocardial dysfunction. Efforts to understand and successfully treat this postresuscitation syndrome are under way.

THE BRAIN DURING AND AFTER CARDIAC ARREST

Support of the brain during the postischemic period is essential to survival after cardiac arrest. Most treatments commonly administered after global brain ischemia have not been formally tested in prospective, randomized clinical trials. Generally accepted postresuscitation therapeutic goals for brain preservation include the following.

Cerebral reperfusion. Maintenance of normal to high cerebral perfusion (based on the individual patient's baseline blood pressure before arrest) is a mainstay of treatment. Normally, cerebral blood flow is autoregulated so that blood flow is independent of perfusion pressure over a wide range of blood pressures (between ~50 and 150 mm Hg, mean arterial pressure). During and after ischemia, autoregulation is compromised, if not lost. Perfusion of ischemic tissue then becomes passively dependent on arterial pressure. As a result, the occurrence of postischemic hypotension compromises cerebral blood flow and may result in significant additional brain damage. Therefore, after restoration of spontaneous circulation, arterial pressure should be rapidly normalized using intravascular volume administration and vasopressors, as needed (137), but may come at the risk of increasing postresuscitation myocardial dysfunction by increasing both preload and afterload.

Ventilation. Although the cerebral circulation may lose its ability to adjust to blood pressure changes after ischemia, responsiveness to arterial carbon dioxide and oxygen levels is usually maintained and may lead to increased intracranial pressure in the presence of hypercapnia or hypoxemia. Hyperventilation may be effective in correcting postischemic tissue acidosis and is important for excretion of the carbon dioxide load generated from bicarbonate administration, which may be given during CPR. Although the usefulness of hyperventilation after global brain ischemia has never been demonstrated, slight hyperventilation is usually recommended after cardiac arrest to guarantee that hypercarbia and the associated increase in intracranial pressure are prevented.

Oxygenation. Adequate tissue oxygenation is necessary to preserve cellular function and to allow postischemic reparative processes to occur. The maintenance of moderate hyperoxia (partial pressure of oxygen [P_{O_2}] >100 mm Hg) seems judicious to prevent transient pulmonary problems from causing a significant deterioration of oxygenation in already compromised tissues. Adequate partial pressure of oxygen in the arterial blood (P_{aO_2}) levels should be maintained using the lowest inspired oxygen fraction (F_{IO_2}) possible with carefully titrated minimal levels of positive end-expiratory pressure. Because hypoxia and hypercapnia must be avoided, controlled ventilation, with muscle relaxation and sedation, if needed, has been recommended for at least several hours after resuscitation.

Correction of acidosis. After brain ischemia, the decline of pH correlates with the extent of cellular necrosis (138,139). Cell damage is further accentuated by hypercapnia and hyperglycemia. Treatment of severe acidosis is generally believed to be clinically beneficial. Because the capacity of respiratory compensation for a metabolic acid load is limited, administration of a buffer base is tempting, but controversial. Unless effectively removed, increased carbon dioxide production from bicarbonate neutralization can lead to intracellular acidosis. Currently, the correction of intracellular acidosis remains a clinical challenge.

Immobilization and sedation. The comatose brain can and does respond to external stimuli, such as physical examination and airway suctioning, with increases in cerebral metabolism. This elevation of regional brain metabo-

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lism requires increased regional cerebral blood flow at a time when the oxygen demand-to-perfusion ratios are, at best, precariously balanced. Protection from afferent stimuli with administration of titrated doses of anesthetic drugs and muscle relaxants may prevent the supply–demand imbalance and improve the chances of neuronal recovery. All activity that increases intracranial pressure, such as straining or coughing, should be suppressed, and tracheal suction should be performed with care.

Anticonvulsant therapy. Seizure activity can increase the cerebral metabolic rate by 300% to 400%. This extreme increase in metabolic demand may tip the tissue oxygen supply–demand balance unfavorably, resulting in additional tissue damage. Although the prophylactic use of anticonvulsant drugs (e.g., before a seizure occurs) is controversial, it is generally agreed that the occurrence of a postischemic seizure should be treated quickly and effectively. Commonly used drugs include barbiturates, benzodiazepines and phenytoin.

Glucose. Postischemic hyperglycemia has detrimental effects on cerebral blood flow, metabolism, edema formation and neurologic outcome (140–142). Thus, after global brain ischemia, hyperglycemia should be avoided and, if present, treated aggressively. The administration of glucose should be avoided, except in cases of verified hypoglycemia.

Corticosteroids. Although steroids are commonly administered to patients with intracranial pathology of any etiology, available clinical studies of steroid use after cardiac arrest suggest no benefit of this therapy (143,144).

Temperature control. The cerebral metabolic rate increases ~8% per degree Centigrade of body temperature elevation. Because the regional cerebral metabolic rate determines regional blood flow requirements, elevation of temperature above normal creates the possibility for a significant imbalance between oxygen supply and demand. Thus, temperature elevation should be treated aggressively in the postischemic period, perhaps aiming at a slightly subnormal body temperature.

Hypothermia, in contrast, suppresses cerebral metabolic activity effectively and has been reported to have a protective effect in global and focal ischemia (145–149). It has been shown experimentally that temperature changes of only 2 to 3°C may limit the extent of ischemic brain injury. Hypothermia, although not yet proven to be of clinical benefit, is probably the most promising brain resuscitation therapy currently on the horizon.

Conclusions. In the quest to improve survival after cardiac arrest, concerns have been raised about the possibility of increasing success in the resuscitation of patients while creating increased numbers of survivors with severe residual neurologic disabilities. However, available outcome data from recent large-scale clinical trials allay these fears (150,151). With very few exceptions, long-term survivors demonstrated recovery of good neurologic function and were able to lead independent lives.

Current rates of survival and recovery of intact neurologic function after cardiac arrest are low. However, there is reason for optimism. Not only are neurons more resistant to ischemia than had been believed previously, but important secondary mechanisms of tissue injury have also been identified. These include generation of oxygen free radicals, increased free intracellular calcium and excessive production of excitatory amino acids and other neurotransmitters. Because these secondary processes occur during postischemic reperfusion, they allow opportunity for clinical intervention. Potentially beneficial agents are now being developed and tested. Unfortunately, none has yet been proven clinically effective.

MYOCARDIAL DYSFUNCTION AFTER RESUSCITATION

Postresuscitation myocardial dysfunction has been recognized by resuscitation researchers for decades. Clinical resuscitation trials have substantiated the importance of postresuscitation myocardial dysfunction and its sometimes fatal outcome. Myocardial postresuscitation dysfunction may manifest itself as fatal recurrent ventricular arrhythmias or persistent low cardiac output and shock. There is laboratory evidence suggesting that the severity of postresuscitation myocardial dysfunction is related to the duration of cardiac arrest, the residual effects of potent vasoconstrictors used during resuscitation efforts and the use of high energy defibrillation.

Experimental evidence of myocardial dysfunction after successful resuscitation has come from a number of independent investigators over the last decade. Decreases in myocardial contractile function and left ventricular compliance after resuscitation after 4 min of VF has been documented in both isolated, perfused rat hearts (152) and in domestic pigs (153,154). Global left ventricular systolic and diastolic dysfunction has been demonstrated in experimental models after 10 to 15 min of untreated VF and subsequent resuscitation. This global dysfunction has been shown to be classic "stunning," with profound mechanical compromise in the presence of normal levels of myocardial blood flow with spontaneous recovery if death does not occur (153).

Treatment and support of myocardial dysfunction after resuscitation is just beginning to be explored. Because left ventricular "stunning" is so reminiscent of what occurs with recently transplanted hearts, similar treatments should be effective. Dobutamine, which is often used to stabilize patients who have had a heart transplant, has been studied in animal models of prolonged cardiac arrest and induced postresuscitation myocardial dysfunction. Left ventricular systolic and diastolic dysfunction improves with dobutamine treatment (155). No survival benefit has yet been established.

Searching for a mechanism of this postresuscitation phenomenon has suggested a role of the potassium adenosine triphosphate channel. Experimental laboratory studies have found less myocardial dysfunction after resuscitation

and increased postresuscitation 48 h survival in animals given a potassium adenosine triphosphate channel activator (cromakalin) (156).

Conclusions. Postresuscitation myocardial dysfunction is a common problem following prolonged cardiac arrest. It appears to be a "stunning" phenomenon and is transient. However, there is substantial morbidity and even mortality associated with this period. An effective approach to treatment of this postresuscitation left ventricular systolic and diastolic dysfunction, once found, has the potential of improving long-term survival from cardiac arrest.

Task Force 2: Acute Coronary Syndromes: Section 2A—Prehospital Issues

Adolph M. Hutter, Jr., MD, MACC, *Co-Chair*, W. Douglas Weaver, MD, FACC, *Co-Chair*

Coronary heart disease (CHD) is the most common cause of mortality for American men and women, accounting for 481,287 deaths in 1995 (8). Annually, an estimated 1,100,000 Americans experience a new or recurrent acute myocardial infarction (AMI) due to CHD, and one-third of them will die from that event (8). Although difficult to quantify, it is estimated that annually 250,000 individuals will die within 1 h of the onset of symptoms and before they reach the hospital owing to cardiac arrest. Out-of-hospital deaths account for more than one-half of all CHD mortality, and many of these victims have no history of CHD (157). Coronary heart disease is prevalent, with ~14 million Americans having a history of myocardial infarction or angina pectoris, or both, with African American men and women bearing a disproportionate burden (158).

Over the past 40 years, there has been a dramatic decline in age-adjusted CHD mortality, which began in the mid-1960s and continues today. From 1965 to 1994, the average age-adjusted CHD decline was 2.8% per year (158). The decline has lessened since 1990 (1.5%). Similarly, although less dramatic, CHD incidence (new cases) and case fatality have fallen, resulting in a rising prevalence of CHD (159–162). These trends have led to a significant increase in the expected life span of Americans (158). Less recognized is the observation that absolute mortality has fallen only slightly, as people still succumb to CHD, although now at older ages.

The postulated reasons for this age-adjusted decline in incidence, case fatality and CHD mortality are many (157,163,164). However, it is clear that traditional risk factor–based prevention and advances in medical therapy for AMI and follow-up care have played an important and increasing role in the decline. The advent of the coronary care unit with intensive monitoring and treatment of complications, along with reperfusion therapies such as thrombolysis, percutaneous transluminal coronary angioplasty (PTCA) and coronary artery bypass graft surgery (CABG), has contributed (157,165–167).

Among the more important goals in early care of CHD is making these effective treatments available to patients in a timely fashion (168). This is obvious for the victim of cardiac arrest, but is also critical in reperfusion and other therapies, where outcomes are improved when treatment is delivered early.

PATIENT DELAYS

Several sources of delay inhibit the early application of beneficial therapies. Widespread availability of these treatments and recognition of the importance of timely application have led to greater scrutiny of sources of delay and programs to reduce delay.

The delay from the onset of symptoms of AMI to definitive therapy (usually reperfusion) is commonly divided into three periods (174). The first is from symptom onset to the patient's action to seek treatment, such as going to the hospital or calling the emergency medical service (EMS). This is the longest component of delay and constitutes from 60% to 70% of the total time.

The first step in this process is teaching patients and their families the basic information they need to live successfully with heart disease and to respond to unexpected symptoms. A summary of educational goals is presented in Table 1 (169–171). Three categories of information are important: 1) practical information; 2) medications; and 3) risk factors. Practical, concrete information is desired by patients more so than detailed descriptions of the mechanism of ischemia (172). This information includes how to avoid a heart attack, what types of symptoms are worrisome and exactly what to do when it is experienced (e.g., stop what you are doing, rest and take up to three nitroglycerin tablets).

Many patients with heart discomfort report that their symptoms were different from the sudden and dramatic event they had expected (175). Longer delays in seeking

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Table 1. Summary of Education/Instruction Goals by Physicians

What Should Be Taught?	Supplemental Materials	How Should Teaching Occur?
Practical, concrete information (e.g., specific symptoms to look for)	Miniature electrocardiographic copies	Timing is important (no more than 15 min)
What to do when experiencing chest discomfort and how to avoid it	Wallet medication cards	Avoid confrontation in preference for empathy (174)
Minimize information on pathophysiology of chest discomfort	Carefully selected brochures	Avoid fear or paternalism
Medication profile	Fifth-grade reading level (173)	Combination of approaches (written and verbal) will help achieve goal
Risk factor modification goals	Videotaped materials for functionally illiterate	Solicit and respond to questions
	Computer health risk appraisals	

treatment have been reported when the expected symptoms did not match the experience (176). This discordance led to a tendency to attribute symptoms to some other source or condition (Finnegan et al., 1998). Women, in general, do not view themselves at risk for a heart attack (Finnegan et al., 1998). Misconceptions such as these need to be suspected and clarified.

The second period is from deciding to seek attention to arrival at the hospital. This is transport time whether by ambulance, automobile or other means and is routinely 3% to 8% of the total delay.

Finally, the time from arrival at hospital to definitive therapy is the third period. Hospital assessment and treatment decision comprises 25% to 33% of the total delay.

The delay period of patient symptom recognition and decision making is long and has undergone considerable study in recent years (177–180). A number of characteristics are associated with longer delay, including older age, female gender, African American race, low socioeconomic group and no insurance. Surprisingly, an important characteristic associated with prolonged delays is a history of CHD or AMI. This counterintuitive observation is unexplained. Environmental factors associated with increased delay include symptom presentation at home, having a spouse at home, being with family members and attempting to contact a physician. Factors associated with decreased delay include symptom severity, typical symptoms and the belief that CHD is preventable. Even when a decision is made to seek medical help, most patients do not dial 911 for EMS transport.

These associations may operate through a variety of individual knowledge, beliefs, attributions and practical barriers to taking action. A patient must recognize the presence of abnormal symptoms, attribute them to a condition requiring medical attention, decide to seek care, arrange transportation and travel to the hospital. Barriers to this process may arise from inadequate knowledge of heart attack symptoms, maladaptive coping strategies, misattribution of the symptoms to noncardiac causes, denial, fear or other characteristics (180,181). Patient denial is a particular issue in those with known CHD. Any attempts to reduce patient delay must confront these many factors.

There are considerable published data on the period for prehospital delay. A review of data from 12 U.S. and European studies published from 1969 to 1987 found that median prehospital delay times ranged from 2.5 to 7 h, with many patients waiting 12 to 24 h or more, with hospital arrival at a time when reperfusion therapy was of unproven benefit. Cooper et al. (182) describe a 6 h median delay time for African Americans in 1983 to 1984. More recently, however, the median delay time of 2.7 h for patients with acute infarction with ST segment elevation in the U.S. was unchanged over a two-year period (183). The Rapid Early Action for Coronary Treatment (REACT) study found a median delay time of 2.2 h at baseline in 20 cities (180).

PATIENT EDUCATION EFFORTS

Prodromal symptoms frequently are present in the days or even weeks prior to the onset of AMI. Educational programs targeting recognition of such symptoms and early action to seek help seem appropriate at this time. Because of substantial patient delays to presentation, attempts have been made to reduce this time. These methods have focused on mass-media strategies supplemented by smaller media and direct patient education. Ho et al. (184) utilized a two-month mass-media campaign using television, radio and newspaper in the Seattle metropolitan area. The median delay time decreased from 2.6 to 2.3 h, which was not statistically significant. Herlitz et al. (185) describe a one-year campaign of mass and specialized media in Sweden using newspaper, printed materials and radio. Patients admitted to the coronary care unit had a statistically significant decline in median delay, from 3.0 to 2.6 h. Those with confirmed AMI had an even greater decrease of 0.7 h. Gaspoz et al. (186), in a one-year mass-media and local media campaign with television, radio, newspapers and printed brochures in Switzerland, also demonstrated a median delay time decrease from 3 to 2.7 h.

Although none of these community studies was ideal in design, much was learned. It appears that a mass-media campaign, which is sustained, intense and supported by other forms of communication, can reduce delay time.

The REACT trial attempted to improve on these design differences with a randomized study of 20 cities with a population of ~100,000 each in a sustained campaign of over one year (180). It improved community awareness of the problem and the proper action to be taken. The median delay time (2.2 h) declined over the intervention; however, similar changes were observed in the "control" communities. Therefore, the differences were not statistically significant. However, there were statistically significant delay time declines in patients who called the 911/EMS system (20%), favoring the intervention communities. Encouragement by physicians to educate their patients with known CHD and those at high risk about reducing delay had little effect. The REACT trial provides evidence that community campaigns to alert citizens and patients of appropriate action for AMI can have an effect. However, a secular trend in delay time suggests the need for new strategies if we are to further reduce this delay. The cost-effectiveness of such programs is unknown.

EMERGENCY MEDICAL SERVICES AND ASSESSMENT OF CHEST DISCOMFORT

Current Emergency Medical Services

Access. Time is a critical factor for the cardiac patient. A single, nationwide emergency number for emergency services—fire, police and health care—is essential, and the number should be the same—911. Today, 911 covers 75% to 80% of the population. There are two types of 911 systems available. One version is the phone number 911, which connects the caller with an operator or dispatcher. A more sophisticated version is the "enhanced 911" system, which has automatic identification of the caller's telephone number and address. This has the advantage that the information required for an emergency response is immediately available. An enhanced 911 system throughout our country should be a goal (187–192). Cellular and digital telephones do not universally have location identification at the present time.

Dispatch. Centralized dispatch is required to provide fast and efficient EMS action. This is particularly important in areas where there are multiple agencies providing services. The dispatcher should be trained to determine what level and extent of services are required. Dispatchers need to quickly determine the nature of the emergency and the types of equipment and personnel required and provide first-aid ("prearrival") instructions over the telephone. It has been shown that untrained telephone callers can be instructed and will perform cardiopulmonary resuscitation (CPR) until the emergency rescuers can respond (190,191,193–198).

Levels of service. The Department of Transportation has developed guidelines for training four different levels of EMS personnel: 1) the first responder; 2) the emergency medical technician (EMT), basic; 3) the EMT, intermediate; and 4) the EMT, paramedic (191,199–202).

First responders with 40 h of training do not transport patients; they provide first-aid for most life-threatening emergencies and may use automated external defibrillators. Firefighters and security guards are often the first responders in the urban areas. In rural and smaller towns, law enforcement officers and volunteers are often the first responders providing treatment. They initiate therapy until another more skilled person or team can assume care and transport the patient (191,199–202).

A basic EMT (EMT-B) has about 120 to 150 h of training in basic first-aid skills. An EMT-B is trained to provide CPR, oxygen therapy and other types of first-aid skills. Most ambulance personnel are EMT-Bs (191,199–202).

The next higher level of training is the intermediate EMT (EMT-I). The amount of training varies from state to state. The Department of Transportation curriculum requires about 450 to 600 h of training and is similar to that of paramedics of a few years ago. The EMT-Is can usually provide intravenous therapy, drug therapy, defibrillation and tracheal intubation. These individuals provide service in rural areas, where it is not feasible to have paramedics (191,199–202).

The paramedic EMT (EMT-P) has the greatest extent of training, ranging from 900 to 1,500 h. Paramedics are trained to differentiate medical emergencies, provide defibrillation, administer cardiac drugs, infuse intravenous fluids and do endotracheal intubation as well as care for many other medical emergencies. Although EMT-Ps are less common than EMT-Bs, they are responsible for transporting the majority of patients in the U.S. (191,199–202).

Types of service. In the U.S., four major types of EMS systems are utilized: city government–based systems, hospital-based systems, public utility systems and competitive private systems (32,76,190,191,199–206).

City government–based systems are most often through the Fire Department. The Fire Department uses fire and rescue officers as dual-trained personnel (fire and medical). In some cities, the Fire Department provides both paramedics and transportation; in others, it provides only paramedics. The Fire Department may provide both basic treatment and transport, as well as a paramedic service (a two-level service system). The Fire Department has advantages by employing personnel with more extensive training in dangerous environments, extrication and rescue. The major potential disadvantage of using the Fire Department is the political environment in which it operates. Fire departments compete for funding with other city services and even within the Fire Department itself. There can be competition within the Fire Department for resources, recognition and promo-

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tion, and at times there are hard feelings between firefighters and EMS personnel. The civil service system can sometimes make discipline difficult.

Police Department EMS systems are usually found in smaller towns. These systems provide first-aid and transport. Adjacent city services generally provide paramedic or basic service with transportation. Often, an adjacent city service is operated as a division of the city hospital. The major advantage of this system is that it circumvents intradepartmental politics and gives EMS the same emphasis as police and fire. A major cost may be housing and locations for the emergency units and for a communications system.

Another system is the hospital-based EMS system. These are generally found in smaller towns where one or two ambulances can service an area from the hospital. Some towns provide a subsidy to the hospital to provide the service.

The public utility model is one in which a single private provider is given a virtual monopoly in exchange for services, similar to that for public utilities. This service provides all ambulance transport, including all contracts with health maintenance organizations or preferred provider organizations, nonemergency transfers and emergency runs. The city frequently has to pay less into this system because nonemergency patient transportation is profitable. Patient charges pay for the system rather than tax dollars.

The final model is the competitive private model. In this model, competing companies either vie for business or are centrally dispatched on a rotating basis. This tends to be the least costly. However, response times can be long, and the level of service may only be basic. This model can lack coordination.

Public service versus business. The bulk of the public service systems is usually paid by the taxpayer, with the individual patient paying only a portion of the cost. Public service systems tend to respond to the victim and obtain only essential information. Thus, most public service systems only obtain adequate billing information for the minority of patients. In contrast, public utility and competitive private systems obtain funding from the patient, with only a small subsidy coming from the city for indigent losses. The bills are itemized with a response fee, a mileage fee for transport and fees for any service rendered, similar to a hospital and physician's bill combined. These systems tend to provide more billable services for a far greater number of patients than do public service systems.

When a system is managed as a public service, there are a number of differences in the service that may not be noticed by the casual observer. A public service system tends to offer uniform levels of service. A public service system will position units so that response time is uniform for most citizens. A system operated as a business will operate the ambulances so that the load per ambulance is similar, which may lead to longer response times in the periphery. Neither the average response times nor the percentage of calls handled within a period may reveal these differences, but they could greatly affect some citizens.

Another difference between the two major approaches is the problem of unusual load requirements. At the time of a rain storm or disaster, business types of systems may not be able to respond as promptly as a public service system, which tends to staff for disaster. Fire Departments often have extra personnel who can be moved quickly from fire suppression to EMS should the need arise.

Business types of systems can respond more quickly to changes in technology, because most new technology can be billed. Because public service systems are a part of the governmental bureaucracy, it can be difficult and time consuming for them to add new technology.

Medical Direction

Strong medical direction must be present for all EMS systems, regardless of the level of care provided, to ensure that patients receive appropriate care and are taken to the appropriate facility. This includes setting patient care standards through protocols. It also includes effective physician or physician-directed input by means of radio or telephone communications where indicated (190,191,200).

PREHOSPITAL ASSESSMENT

Prehospital identification of patients with AMI. The primary purpose for prehospital 12-lead electrocardiographic (ECG) diagnostic programs is the early detection of AMI with ST segment elevation (207), and communication of that information to the receiving emergency physician before patient arrival. Multiple studies have shown the feasibility of performing prehospital 12-lead ECGs (208,219). Diagnostic-quality ECGs can be acquired and successfully transmitted in about 4 min in ~85% of patients eligible for 12-lead electrocardiography (210,211,215,216).

It has been demonstrated that prehospital 12-lead ECGs improve prehospital diagnostic accuracy for patients with a final hospital diagnosis of AMI, angina or nonischemic chest pain (210). For patients with a final hospital diagnosis of AMI in one study, the specificity of the base physician's prehospital working diagnosis (incorporating both paramedic-acquired history and a prehospital 12-lead ECG) was improved from 68% to 95%, and the positive predictive value increased from 33% to 71%, as compared with single-lead telemetry (210). When the 12-lead ECG alone was used by base physicians to diagnose AMI, sensitivity was 42%, specificity increased to 99.7% and positive predictive value increased to 97%, demonstrating that the prehospital 12-lead ECG alone was more accurate in the prehospital diagnosis of AMI than the ECG and historic information (210).

The direct impact that improved prehospital diagnostic accuracy has on treatment and outcome for patients with

AMI, angina and nonischemic chest discomfort remains to be fully characterized.

Reduced hospital-based time to treatment. Many studies have demonstrated significant reductions in hospital-based time to treatment with reperfusion therapy for patients with AMI identified before patient arrival (213,215,216,220). Time savings in these studies ranged from 20 to 55 min (213,215,216,220).

A similar time reduction was demonstrated by transmitting the prehospital 12-lead ECG directly to the receiving hospital (215). Different methods of patient transport and communication of diagnosis have also been assessed (216). The median hospital delay to treatment in one such study was 64 min for patients transported by private automobile, 55 min for patients transported by local ambulance, 50 min for patients transported by the EMS with a prehospital ECG obtained but not transmitted to the receiving hospital and 30 min for patients transported by the EMS with a 12-lead ECG transmitted from the field (216).

These data support the contention that prehospital identification of patients with AMI reduces hospital-based door-to-drug time and assists receiving hospitals in meeting the National Heart Attack Alert Program's recommendation of treatment within 30 min of arrival (187).

The management and outcome of patients receiving and not receiving prehospital 12-lead electrocardiography were evaluated in the National Registry of Myocardial Infarction-2 data base (221). Although the median time from infarct onset to hospital arrival was longer among those having a prehospital ECG, this group experienced a significantly shorter median time to initiation of either thrombolysis or primary angioplasty. The prehospital ECG group was also more likely to receive thrombolytic therapy, primary angioplasty or CABG. The in-hospital mortality rate was 8% in patients with a prehospital ECG and 12% in those without a prehospital ECG ($p < 0.001$). Investigators concluded that the prehospital ECG is a valuable test that is underutilized nationally.

Identifying thrombolytic candidates by checklists. Patients with AMI identified by a prehospital 12-lead ECG can be further classified as thrombolytic-eligible candidates through the use of a checklist. Prehospital thrombolytic therapy trials provide experience that appears to be useful in reducing time to treatment (212,217,222–228). In the U.S., paramedics, not physicians, have used checklists to identify thrombolytic candidates (209,215,219,220,229). One U.S. study directly addressed the accuracy of a paramedic contraindication checklist (209). The positive predictive value of case selection was 100%. Paramedic scene time was increased by only an average of 4 min (209).

These data support the feasibility, accuracy and time-effectiveness of prehospital identification of thrombolytic candidates through focused contraindication checklists. Such a checklist should be part of the prehospital assessment of all patients with chest discomfort, as recommended in the American College of Cardiology/American Heart Association's Guidelines for the Management of Patients with Acute Myocardial Infarction (230).

Computerized ECG programs. Several computerized ECG programs have potential to assist in improving prehospital AMI diagnostic accuracy and clinical decision-making.

Electrocardiographic criteria for the automated ECG diagnosis of AMI has been evaluated using the 12-SL interpretive algorithm (Marquette Medical Systems, Inc.) (218). This automated program diagnosed acute evolving Q wave myocardial infarction with 71% sensitivity and 98% specificity. Specificity was 100% when patients with a known previous Q wave myocardial infarction were excluded.

In another large study, the positive predictive values of the computer- and physician-interpreted ECG were 94% and 86%, respectively, and the negative predictive values were 81% and 85% (231). Computerized ECG algorithms are not all the same and should be prospectively validated before implementation (232,233).

Predictive instruments. The Acute Cardiac Ischemia Time-Insensitive Predictive Instrument (ACI-TIPI) has been prospectively validated for use in the Emergency Department (234) and retrospectively validated for prehospital use (235). This predictive instrument is incorporated into a computerized electrocardiograph. Using the patient's age, gender and presence or absence of chest discomfort on presentation, the ACI-TIPI predicts the likelihood of acute cardiac ischemia (AMI or angina), along with the ECG. In one study, the ACI-TIPI was associated with a reduction in false positive diagnoses and reduced the number of hospital admissions among patients without acute ischemia (234).

PREHOSPITAL STUDIES OF FIBRINOLYTIC THERAPY

Several studies have reported results of trials of fibrinolytic therapy initiated before hospital admission. Most have been designed to evaluate time savings, resulting left ventricular function, infarct size and mortality differences in patients treated in the prehospital setting as compared with in-hospital treatment. In an early, small, randomized Israeli trial of prehospital versus in-hospital treatment aimed at evaluating left ventricular function, there was no difference in resulting ejection fraction despite a 43 min time difference between the groups. Mortality was also similar (228). The findings from this, as well as other, studies led to several randomized, controlled trials. The largest trial—the European Myocardial Infarction Project (EMIP)—was carried out in 15 European countries and Canada. Anistreplase was given as a bolus in the prehospital setting to 2,750 patients, and their outcomes were compared with those of 2,719 patients treated in the hospital (222). Although the project initially planned to enroll 11,000 patients to have sufficient statistical power to show a 3% difference in